MYCOSPORINES-LIKE AMINO ACIDS (MAAS) FROM DIATOMS: *IN VIVO* FUNCTIONS AND DRUG DISCOVERY APPLICATIONS

PhD Student: Saverio Savio/ *Supervisor*: Dr. Roberta Congestri

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Diatoms, a highly diverse group of unicellular microalgae, ≈10^6 species, encased in nanoporous silica cell walls, are key players in aquatic food webs. They contribute up to 40% primary production in marine coastal areas, due to efficient nutrient uptake, rapid growth rates and chemical defense strategies. Indeed, diatoms produce polyunsaturated aldehydes and domoic acid against copepod predators(Haroardóttir et al., 2019; Pohnert, 2005). This bioactive potential has raised industry interest, for polyunsaturated fatty acids enriched aquafood and fucoxanthin extraction for pharmaceutics (Bozarth et al., 2009; Wang and Seibert, 2017).

Our previous work showed that extracts obtained from mass cultivated diatoms, three phylogenetically and ecologically diverse strains, one native and two commercial model organisms, exhibit cytotoxic and anti-proliferative effect on human melanoma cell lines. A preliminary analysis evidenced the presence of small hydro-soluble molecules in the extracts, attributable to mycosporine-like amino acids (MAAs). These small secondary metabolites, produced across a variety of organisms, display strong UV-absorbing properties, are involved in oxidative and osmotic stress protection, intracellular nitrogen storage and chemical signalling (Carreto and Carignan, 2011; Oren and Gunde-Cimerman, 2007). To date, scant knowledge exists on MAA synthesis in diatoms and their *in vivo* function.

The main goal of this PhD project is to verify whether selected diatom strains are able to produce MAAs, to circumscribe their identity and to characterize their role *in vivo.*

The scientific hypothesis is that MAAs synthesis may respond to different environmental conditions and be affected by the interplay between diatom silica cell walls, frustules, and light. In fact frustules, whose shape and pore patterns are species-specific and finely controlled, have shown to protect cells from harmful radiation too (Ellegaard et al., 2016; Ingalls et al., 2010).

To validate our hypothesis, I will: mass cultivate strains, selected to incorporate most of frustule, ecologic and phylogenetic diversity, at standard conditions; extract the obtained biomass; assess MAAs presence, identity and quantity by means of NMR or/and LC-MS approaches. Then, I will manipulate culture conditions by exposure to different irradiances, monochromatic lights, UV radiation and applying osmotic or nitrogen nutrition stresses, in order to evaluate relationships between MAAs production and diatom physiological response. Co-culture experiments will be also performed to assess MAAs potential role as chemical signals.

A second goal will address the drug discovery applications of the extracts, analysing their bioactivity, dissecting the molecular pathway activated on human melanoma cell lines, and evaluating the anti-obesity and anti-diabetic potential on brown adipose tissue.

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